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## FULL-LENGTH ORIGINAL RESEARCH

# Impaired social attention detected through eye movements in children with early-onset epilepsy

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## Abstract

**Objectives:** Children with early-onset epilepsy (CWEOE; epilepsy onset before 5 years) exhibit impaired social functioning, but social attention has not yet been examined. In this study we sought to explore visual attention via eye tracking as a component of social attention and examine its relationship with social functioning and Autism Spectrum Disorder (ASD) risk scores.

**Methods:** Forty-seven CWEOE (3–63 months) and 41 controls (3–61 months) completed two eye-tracking tasks: (1) preference for social versus nonsocial naturalistic scenes, and (2) face region preference task. ASD risk was measured via the Modified Checklist for Autism in Toddlers or Conners Early Childhood Total Score. Social functioning was assessed via the Greenspan Social-Emotional Growth Chart, or Infant-Toddler Social & Emotional Assessment Competence Scale, or Conners Early Childhood Social Functioning Scale, depending on age. Fixation preferences for social scenes and eyes were compared between groups and evaluated by age and social functioning scores.

**Results:** Regression analysis revealed that CWEOE viewed the social scene to a significantly less degree than controls. The greatest difference was found between the youngest CWEOE and controls. Fixation duration was independently and significantly related to social functioning scores. There were no significant differences between CWEOE and controls in the face scanning task, and there was no significant relationship between either task and ASD risk scores.

**Significance:** CWEOE exhibit task-specific atypical social attention early in the course of the disease. This may be an early marker of impaired social development, and it suggests abnormal social brain development.

## KEYWORDS

Autism Spectrum Disorder, eye tracking, infant, social functioning

## 1 | INTRODUCTION

Children with early-onset epilepsy (CWEOE; epilepsy onset before 5 years) exhibit impaired social functioning,<sup>1,2</sup> but to what extent is *social attention* compromised in CWEOE, and if this is related to social functioning, is unknown. Social attention mediates language development, theory of mind, and social functioning (defined here as social-emotional development and peer relationship skills), in children,<sup>3-6</sup> and although no strict definition exists,<sup>7</sup> it can be understood as the attentive, cognitive, and -processes that occur in response to social information. Detection of abnormal social attention may offer insight toward the pathogenesis of social dysfunction in CWEOE, and it could help identify those at risk of social behavior problems.

Social attention can be examined through eye movement analysis during visual attention toward social stimuli. The orientation, focusing, and disengagement of visual systems in response to social stimuli is a fundamental facet of social attention.<sup>7</sup> These processes develop over the course of early childhood, as is demonstrated through preferences for faces over nonfaces in newborns,<sup>8</sup> following the gaze of others in infancy,<sup>9</sup> and by the development of joint attention by toddlerhood.<sup>4</sup> Abnormalities in socially attentive processes are evident in clinical groups associated with negative social outcomes such as Autism Spectrum Disorder (ASD), where atypical visual attention toward people and faces is well documented.<sup>10,11</sup> Examining visual attention in childhood epilepsy is of particular relevance given that social behavior problems, ASD, and social functioning difficulties are overrepresented.<sup>12-14</sup>

Eye movement analysis is captured using eye-tracking technology, which has been employed extensively in typical and atypical childhood development research.<sup>15</sup> It has been particularly prevalent in ASD. For instance, previous research has shown that compared to typically developed persons, children and adults with ASD are slower to orient toward, and spend less time fixating upon, people within naturalistic scenes.<sup>16,17</sup> When viewing faces, Chawarska and Shic<sup>18</sup> reported that children with ASD spent more time looking at peripheral features of the face (ie, hair, cheeks, and forehead) compared to central features (ie, nose, mouth, eyes), when compared to typically developing children. Atypical visual attention toward faces has also been evident in other clinical conditions prone to social difficulties, including fragile X syndrome<sup>19</sup> and preterm children.<sup>20</sup> It is notable that attention to faces is a relevant indicator of social development, even within typically developing children, where time spent fixating the face and eyes has previously been associated with level of social functioning.<sup>6</sup> Thus eye movement analysis of social attention may provide a psychophysiological indicator of social development applicable to all children.

### Key Points

- Social attention is compromised in children with early onset epilepsy (CWEOE)
- CWEOE exhibit reduced attentional priority and importance toward naturalistic social scenes compared to controls
- Abnormal social attention evident early in the course of the disease
- CWEOE view faces similarly to controls
- Abnormal social attention is a potential early marker of poor social cognitive development in CWEOE

Eye movement analysis of social attention in childhood epilepsy has been scarce, although atypical visual attention toward faces in adolescents with epilepsy as well as epilepsy-related Rett syndrome has been reported.<sup>21-23</sup> In adolescents, Lunn et al<sup>21</sup> found slower gaze processing toward emotional expressions that was independently associated with epilepsy, with the authors suggesting that age at epilepsy onset could be associated with age-dependent social skill acquisition. Social attention status in CWEOE has not been investigated to our knowledge, despite early childhood being a key period in fundamental neural and social development.<sup>24,25</sup> An examination of social attention may provide insight into the early nature of social functioning problems in childhood epilepsy.

In this study we sought to explore visual attention as a component of social attention and its relationship with social functioning and ASD risk scores in CWEOE compared to controls. Because social functioning problems are common in childhood epilepsy<sup>12</sup> we hypothesized that CWEOE would display reduced attentional priority (ie, first location of eye gaze fixation), and/or reduced attentional importance (ie, total fixation duration) to social scenes and face regions compared to typically developing control children.

## 2 | METHODS

This case-control study partnered the NEUROPROFILES study, in which the recruitment strategy and inclusion and exclusion criteria, were described previously.<sup>1</sup> Briefly restated here, NEUROPROFILES was a prospective population-based study of CWEOE and neurologically healthy controls, recruited from South East Scotland, between May 1, 2013 and June 30, 2015. In the current study, participants included those recruited into NEUROPROFILES as well as Scottish resident children identified through the same identification and recruitment strategy but who were not population-based.



CWEOE and controls were up to 59 months of age at the time of epilepsy diagnosis or identification, respectively.

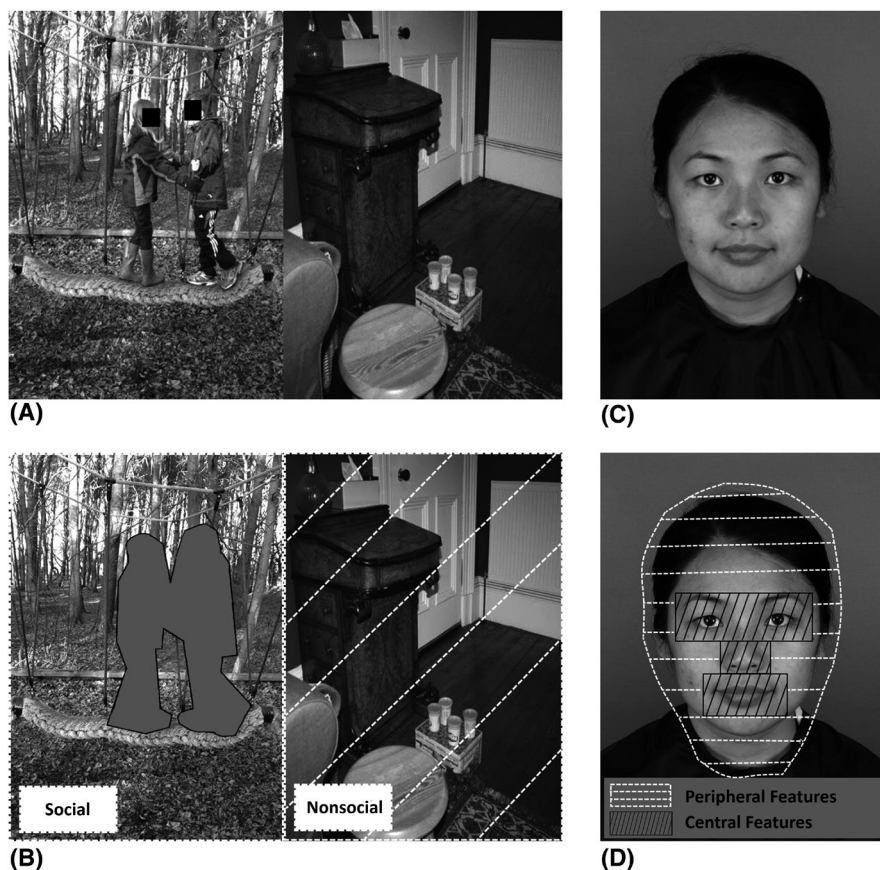
## 2.1 | Neurobehavioral assessment

All children completed a neurobehavioral assessment followed by an eye-tracking battery, described previously.<sup>1</sup> Neurobehavioral assessment tools were selected a priori to evaluate two domains: social functioning (ie, social-emotional development and peer relationship skills), and risk of ASD. To compare CWEOE and controls across the 1–59 month age spectrum, where different age-appropriate tests are used, assessment tools were pooled by domain. This method was applied previously.<sup>1</sup> The social functioning domain consisted of The Greenspan Social-Emotional Growth Chart (1–11 months), Infant-Toddler Social & Emotional Assessment (ITSEA) competence scale (12–23 months), and Conners Early Childhood (CEC) Social Functioning scales (24–59 months), which were converted to T scores with an increasing score reflecting increased social functioning difficulties. In the ASD risk score domain, because no continuous variable is generated for the Modified Checklist for Autism and toddlers (MCHAT) for children 16–23 months, only the Social Responsiveness Scale 2 (SRS2, 24–59 months) T scores were used for analysis. To include an assessment of ASD risk for all children from 16 months of age, children

were categorized into high or low risk of ASD based on a MCHAT “high risk” score or a SRS2 Total Scale T-score of  $\geq 65$ . General cognitive ability was poorer in CWEOE compared to controls in the NEUROPROFILES study; therefore general cognitive ability was used as a confound variable applying the same approach described above. That is, Bayley III Cognition (1–29 months) and wechsler preschool & primary scale of intelligence (WPPSI) III full scale intelligence quotient (FSIQ) (30–59 months) scores were converted to *z* scores, with decreasing scores indicating poorer cognition.

## 2.2 | Eye-tracking materials and procedures

Two eye-tracking tasks of visual attention were used to evaluate social attention: (1) social scene preference and (2) face region preference. The social scene preference task has been validated previously in typically developing and preterm infants<sup>20,26</sup> and assesses visual preference for competing social and nonsocial naturalistic scenes. Stimuli for the social preference task consisted of six real-world scenes with two versions of each: one with one to two children (ie, social), and one without children (ie, nonsocial). Each trial paired a social and nonsocial scene presented side by side (Figure 1), with a combined on-screen size of  $24.0 \times 17.0$  cm. There was a total of 12 trials. Each trial was presented for 5000 ms with an interstimulus interval (ISI) of 4000 ms. The face region



**FIGURE 1** Task examples and areas of interest (AOIs). Social preference task (A) (faces hidden for publication only). AOIs were divided into two equal halves (B), with additional child/children (B, gray area) and head region (AOI not shown) AOIs. Face region preference task (C). AOIs were analyzed by central versus peripheral facial features (D), with further analysis of the eyes vs mouth regions

preference task evaluated preference for facial regions during free-viewing of photographs of human faces.<sup>20,26</sup> The task comprised six photographs of adult faces (three male and three female) displayed on a blue background selected from the two-dimensional (2D) face database at the University of Stirling (<http://pics.psych.stir.ac.uk>). Emotional expressions and direction of eye-gaze influence facial and neural processing.<sup>27,28</sup> Therefore, and in line with previous studies,<sup>18,20</sup> emotionally neutral faces with direct gaze were selected as an elementary measure of face processing. Photographs were displayed on the screen at 16 × 21.5 cm. The task included six trials, each lasting 10 000 ms with an ISI of 4000 ms.<sup>26</sup>

Eye movements were detected using a Tobii x60 eye-tracker. Stimuli were presented in Tobii Studio 3.2.2 and displayed on an LCD monitor with a screen size of 40.8 × 25.0 cm and resolution of 1440 × 900 pixels. Children sat alone or on their parent's laps 50–60 cm from the monitor. No task-specific instructions were given in order to maintain standard operating protocol for verbal and nonverbal children. Trials were viewed in a random order across two blocks. Visual acuity and visual field were assessed as a control measure using Keeler Acuity Cards (Keeler Ltd.), and a locally developed visual field test,<sup>29</sup> respectively. Eye tracker fixation parameters, calibration procedures, data quality procedures, image-wise analysis, and a statistical analysis of attentiveness to the eye-tracking battery are detailed in the Appendix S1.

### 2.3 | Eye movement metrics and statistical analysis

Fixation data were captured on predefined areas of interest (AOIs) (Figure 1). AOIs for the social preference task encompassed the entire social and nonsocial scene images. AOIs were also created for children and head regions within the social scene to validate within-scene preferences for children, and to explore head preference.<sup>30</sup> AOI selection on the face scanning task was founded on Chawarska and Shic,<sup>18</sup> and was created for central facial features (ie, eyes, nose, and mouth) and peripheral facial features (ie, hair, ears, forehead, cheeks, and neck).

Total fixation duration (TFD) and time to first fixation (TTFF) metrics were extracted from Tobii Studio. TFD captures the total time spent fixating on any given AOI across the duration of trials, reflecting attentional importance.<sup>31–33</sup> To account for off-screen or non-AOI looks across trials, TFD was expressed as a proportion of the total time spent fixating the whole stimulus. TTFF measures the time taken to first view an AOI and is a proxy for attentional priority.<sup>17</sup> Although TTFF alone can be used to assess attentional priority, it can be argued that using averaged raw TTFF data across trials to assess which AOI subjects attended to first

is liable to bias. Across  $k$  trials, disproportionately small or large latencies can distort the latency of the sample mean. It is, therefore, more accurate to use TTFF to determine the AOI viewed first in each trial, and to record the total number of first viewed AOIs across trials as a discrete variable. This can then be expressed as a proportion (eg, if AOI 1 was viewed first six times from 10 trials, then this AOI would be preferred 60% of the time).

Statistical analyses were performed on IBM SPSS Statistics for Windows, Version 21.0.0 (IBM Corp., Released 2012). Normality was assessed according to Shapiro-Wilk test and upon visual inspection of histograms and QQ plots. Mean TFD data from the social preference task were normally distributed but were non-normally distributed from the face region preference task. Mean differences (MDs) and 95% confidence intervals (CIs) were reported when possible. Interquartile ranges (IQR) and effect sizes were reported for non-normally distributed data.

Using the above metrics, we sought to determine social attention in CWEOE compared to controls as demonstrated through preferences toward social/nonsocial scenes, and face regions. One-sample  $t$  tests were conducted to determine (1) the mean proportion of first looks toward the social scene, and (2) the mean TFD toward the social scene, compared to chance levels (test value of 0.50) in CWEOE and controls separately. In the face-region preference task, a Wilcoxon signed-rank test was used to assess (1) the ranked mean proportion of first looks toward the central facial features compared to peripheral facial features, and the ranked mean proportion of first looks toward the eye region compared to the mouth region, and (2) the ranked mean TFD toward central facial features compared to peripheral features, and the ranked mean TFD toward the eye region compared to the mouth region. Independent sample  $t$  tests were applied for between-group (ie, CWEOE versus controls) analysis of mean TFD toward the social scene in the social preference task, whereas Mann-Whitney  $U$  tests were applied to between-group (ie, CWEOE vs controls) analysis of ranked mean TFD to central facial features, and eye region, in the face region preference task. An independent-sample  $t$  test was used to evaluate TFD in children  $\geq 16$  months with high vs low ASD risk.

To evaluate the relationship between social attention and social functioning or ASD risk scores, mean TFD toward the social scene (social preference task) and ranked mean TFD (face region preference task) toward the eye region, were correlated with social functioning T scores and SRS2 T scores (ie, ASD risk score) using Pearson or Spearman rank correlations, depending on the distribution of the data. Hierarchical multiple linear regressions were conducted to explore contributions of variables significant at the  $p < .05$  level during univariable analyses, with mean TFD toward the social scene in the social preference task.

### 3 | RESULTS

Forty-seven CWEOE (32 male; median age 37, range 3–63, months) and 41 (19 male; median age 27, range 3–61, months) controls were enrolled in the current study; there were no intergroup difference between CWEOE and controls according to gender or age. No child with successful eye-tracking calibration had visual acuity or visual field deficit. CWEOE and controls attended to the eye-tracking tasks similarly (see Appendix S1). Epilepsy and syndromic classifications of CWEOE are presented in Table 1, with further details provided in Appendix S1.

Controls (mean .52, standard deviation [SD] .85) had higher general cognitive ability (ie, Bayley III Cognition or WPPSI III FSIQ) *z*-scores compared to CWEOE (mean  $-.28$ , SD .89). CWEOE (T score 55.02, SD 11.56), and controls (T score 51.26, SD 10.51) had similar levels of social functioning (SEGC, ITSEA Competence, or CEC social functioning);  $t(79) = 1.53$ ,  $p = .1$ , although CWEOE (T score median 49.0, IQR 18) over 24 months ( $N = 26$ ) had higher SRS2 scores than controls ( $N = 27$ , T score median 41.5, IQR 8);  $z = -2.61$ ,  $p = .009$ , and 6 of 35 CWEOE aged  $\geq 16$  months had a high risk of ASD (ie, MCHAT High Risk or SRS2 T Score  $\geq 65$ ). No control ( $N = 27$  aged  $\geq 16$  months) was deemed at high risk of ASD.

**TABLE 1** Epilepsy or syndromic classification—structure adapted from Berg et al<sup>50</sup>

Classification	N (%)
1. Electroclinical syndromes	
Infantile spasms/West syndrome	2 (4.3%)
Benign infantile epilepsy	4 (8.5%)
Generalized epilepsy with febrile seizures +	2 (4.3%)
Panayiotopoulos syndrome	1 (2.1%)
Genetic generalized epilepsy	
Childhood absence epilepsy	6 (12.8%)
GGE with GTCS	5 (10.6%)
GGE—other	1 (2.1%)
Rett syndrome	1 (2.1%)
2. No identified electroclinical syndrome	
2.1 Epilepsies with known cause	
Genetic focal epilepsy due to single gene mutations	2 (4.3%)
Focal epilepsies attributed to structural causes	5 (10.6%)
Generalized epilepsy attributed to structural causes	1 (2.1%)
2.2 Epilepsies of unknown cause	
Generalized epilepsy of unknown cause	10 (21.3%)
Focal epilepsy of unknown origin	6 (12.8%)
Unclassified	1 (2.1%)

#### 3.1 | Task 1 - Social preference

Data for three control children were excluded from the analysis due to limited data capture for this task (ie, less than 33% of trials captured). CWEOE ( $N = 47$ ) and controls ( $N = 38$ ) looked first toward the social scene more often than the nonsocial scene and exhibited longer mean TFD toward the social scene than the nonsocial scene, with control children doing so to a greater degree than CWEOE (Table 2). Thus CWEOE and Controls demonstrated both an attentional priority and attentional importance toward the social scene, albeit stronger in controls. TFD to the social scene significantly decreased with increasing age in controls ( $r = -.54$ ) but there was no significant relationship observed in CWEOE. Social Functioning score was significantly moderately correlated with TFD to the social scene ( $r = .29$ ) but neither general cognitive ability nor ASD risk scores (ie, SRS2 T scores) were correlated with TFD to the social scene. There were no significant differences in mean TFD for CWEOE at risk of ASD ( $N = 6$ ) vs those not at risk ( $N = 29$ ) (MD .04 [ $-.13$ , .05],  $p = .34$ ). Therefore, social functioning scores but neither general cognitive ability nor ASD risk scores were included in multiple linear regression analysis.

In the multiple regression analysis group (CWEOE vs controls), age and social functioning T scores remained independently significant ( $F(4,73) = 8.68$ ,  $p < .001$ ) (Table 3); in CWEOE, TFD toward the social scene was significantly less than controls, whereas mean TFD toward the social scene decreased with increasing age. A significant group-age interaction was observed; this revealed that control children exhibited a higher TFD toward the social scene in infancy, which reduced with increasing age, whereas mean TFD in CWEOE was lower in infancy and remained stable across age (Figure 2). Poorer social functioning was independently associated with increased mean TFD toward the social scene.

Examination of TFD toward the children in the social scene only demonstrated that although CWEOE were drawn less to the social scene itself, when they did, they spent a similar proportion of time fixating the child (TFD mean difference =  $-0.06$ , 95% CI  $-0.13$ ,  $0.02$ ) or head regions (TFD mean difference =  $.003$ , 95% CI  $-0.06$ ,  $0.07$ ) as controls.

#### 3.2 | Task 2 - Face scanning

One CWEOE had limited data capture for this task ( $<20\%$  of trials) and was excluded from analysis. CWEOE ( $N = 46$ , median 67% of trials, IQR 40–83) and controls ( $N = 41$ , median 75% of trials, IQR 33–83) significantly fixated the central facial features (ie, eyes, nose, and mouth) first more often than peripheral features or image background. Likewise, both CWEOE and controls fixated the central features significantly longer than would be expected by chance alone

**TABLE 2** First fixation and total fixation duration (TFD) to social scene in CWEOE and Controls

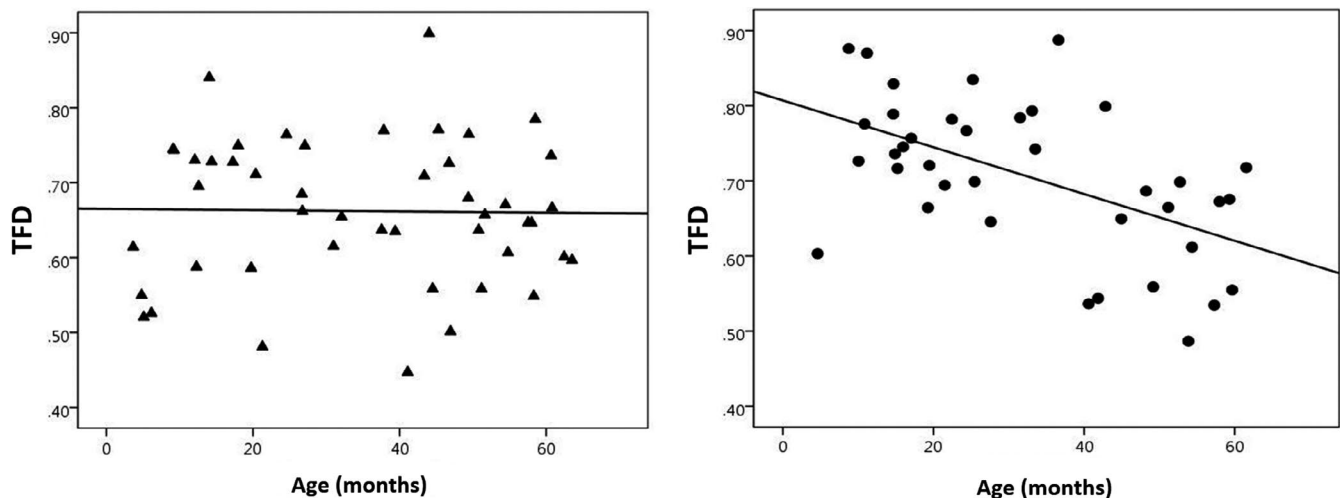
	Number of trials social scene fixated first	TFD (proportion) on social scene
Controls	73.5%	0.71
CWEOE	66%	0.66
	$p < .05$ (MD 4.39; 95% CI .11, 8.66)	$p < .05$ (MD .08; 95% CI .02, .13)

Abbreviations: CI, confidence interval; MD, mean difference.

(0.34), or when compared to peripheral features (ie, neck, chin, cheeks, ears, forehead, and hair) (Table 4); CWEOE,  $z = -4.45$ ,  $p < .001$ ,  $r = .66$ , and controls,  $z = -4.52$ ,  $p < .001$ ,  $r = .71$ . There was no significant difference in TFD to central or peripheral facial features between groups.

When analysis focused on fixations toward the eyes and mouth only, both CWEOE ( $z = -3.25$ ,  $p < .01$ ,  $r = .48$ ) and controls ( $z = -2.48$ ,  $p < .05$ ,  $r = .39$ ) looked first more often at the eyes compared to the mouth, and looked significantly longer at the eyes compared to the mouth (CWEOE,

	$\beta$	95% Confidence Intervals		$p$ -Value
		Lower	Upper	
Constant	0.69	.57	.81	<.001
Group: Controls vs CWEOE	−0.18	−0.27	−0.1	<.001
Age (months)	−0.003	−0.01	−0.002	<.001
Group × Age interaction	0.004	.001	.006	.001
Social functioning T score	0.003	.001	.005	.004

**TABLE 3** Multiple linear regression of factors associated with total fixation duration (TFD) to social scene**FIGURE 2** Total fixation duration (TFD) and age in children with early-onset epilepsy (CWEOE; triangles) and controls (circles)**TABLE 4** Proportion of total fixation duration (TFD) for facial features in CWEOE and controls

	Central features	Peripheral features	Image background	Eyes	Mouth
	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)
CWEOE	0.71 (0.43–0.84)	0.18 (0.11–0.31)	0.08 (0.03–0.15)	0.60 (0.32–0.85)	0.12 (0.03–0.37)
Controls	0.72 (0.41–0.80)	0.21 (0.13–0.30)	0.07 (0.04–0.20)	0.51 (0.18–0.77)	0.16 (0.06–0.41)

Note: No significant between-group differences observed.



$z = -3.90$ ,  $p < .001$ ,  $r = .58$ ; controls,  $z = -2.88$ ,  $p < .01$ ,  $r = .45$ ) (Table 4). There were no significant between group differences in first fixation preference or TFD toward the eyes or mouth.

There were no significant correlations between TFD toward the central facial features, or eyes, and age, in either CWEOE or controls. Similarly, there were no significant correlations between TFD and general cognitive ability, SRS2 score, or social functioning T scores.

## 4 | DISCUSSION

This study examined social attention in CWEOE via visual attention to social stimuli. The main findings revealed that CWEOE exhibited abnormal social attention in contrast to typically developing children. This finding was task specific and was observed during the social preference task but not the face region preference task, where CWEOE viewed facial features in a pattern similar to that of controls. Given that both CWEOE and controls attended similarly to the eye-tracking battery overall (see Appendix S1), the findings are unlikely to be due to any generalized impairment in attention.<sup>1,12</sup> Fixation time was found to be related to social functioning, providing support that changes in social attention were reflective of immature social development. Overall, the data provide evidence that social attention is adversely affected in children with epilepsy during the first years of life, which may be a risk factor for abnormal social development.

The social preference task was sensitive to maturity of social cognitive development, as reflected by the relationship with social functioning scores and age and evidenced by poorer social attention particularly in younger CWEOE. Poorer social functioning was associated with increased fixation duration toward the social scene compared to the nonsocial scene. The reason for this relationship is unclear but we speculate that it may reflect an increase in required processing time that is more typical in a younger age of social development or may be a reflection of individual variation along a spectrum of social cognitive development.<sup>34</sup> The task was more sensitive to social attention with earlier age as demonstrated in control children, where fixation duration to the social scene naturally reduced with increasing age. Again, this is presumably reflective of more efficient social processing with age.<sup>35-37</sup> Thus more processing time would be required in infancy but less in preschool aged children. CWEOE fixated the social scene longer than the nonsocial scene, indicating they were more drawn toward social stimuli overall, but they did so significantly less than control children, reflecting a weaker attraction to social stimuli than should be expected. This reduction in attentional priority for socially relevant stimuli in the absence of a clear interaction between group and social functioning T scores, suggests that,

like in previous reports,<sup>21</sup> epilepsy itself has an independent and adverse impact on the development of the social brain in early life. Fixation duration to the social scene remained stable across age in CWEOE, and thus the clearest disparity in social attention was observed in the youngest CWEOE. It remains unclear why this disparity did not continue to be evident in preschool-aged children but may have been due to a lack of social attentive sensitivity for older children of the task itself, or that the later development of epilepsy may have bypassed any relevant periods of social cognitive development as captured by this task. Nevertheless, the findings indicate that social attention is compromised in CWEOE and that this reflects immature social development. Because the CWEOE were examined ~2.6 (SD 2.5) months following a diagnosis of epilepsy, it can be concluded that abnormal social attention occurs very early in the course of the disease. It should be noted that epilepsy, age, and social functioning scores accounted for only 29% of the variance in fixation duration toward the social stimuli during regression modeling, and other yet-unknown variables must contribute toward eye movement behavior during this task.

All children in this study preferred viewing the central features of the face, specifically the eyes, when compared to other facial features. This replicated previous findings in infants and preschool children,<sup>18,20,26</sup> and offers validity of the task in this cohort. Because faces with neutral expression and gaze were used, the task may not have been sufficiently socially complex to identify children with poor social functioning. Several studies have found impairments in facial recognition and identification of emotional expression in childhood and adult epilepsy syndromes.<sup>38-41</sup> Deficits such as these can be reflective of developmental disorders or social communication difficulties,<sup>40,42</sup> suggesting more socially complex tasks may be required to elicit abnormal eye movements toward faces should they exist in CWEOE.

Eye movements during the social preference task and face region preference task were not associated with risk of ASD. Several studies have reported typical visual scanning of static neutral faces in children and adults with ASD.<sup>43-45</sup> Thus children with ASD, or at higher risk of ASD, appear to be drawn in a similar way to socially salient features as are typically developing children. However, eye movements may begin to deviate from normal when nonstatic stimuli are used,<sup>45,46</sup> suggesting that static neutral faces have much less social sensitivity and may be less useful at identifying those with impaired social attention. The lack of social sensitivity to static neutral faces may also explain why CWEOE displayed social attention abnormalities during the scene preference task but not the facial regions task.

The social functioning construct used in this study was a reflection of social skill development, peer relationships, social engagement, and social temperament. Given that those at high risk of ASD in this study did not exhibit abnormal

social scene preference or face region preference, the findings provide some support that this task may have measured a different social attentive construct than that affected in children with ASD. However, ASD assessment tools are age limited and not all the CWEOE in the cohort could be evaluated with a screening instrument. Secondly, ASD screening tools may have limited specificity,<sup>47,48</sup> and the findings here were derived from CWEOE with early ASD-type behaviors but not clinically diagnosed ASD. Thus any generalizability to ASD is limited. It would be informative to investigate longitudinal cohorts on similar eye-tracking social paradigms including children with diagnosed ASD. Future research in CWEOE, on the face scanning task specifically, could investigate dynamic stimuli and emotional expression recognition.

The number of standardized tools available for preschool children are limited,<sup>49</sup> and although tools of similar theoretical construct and/or convergent validity were selected, some differences between test constructs were likely to have existed. Future studies examining focused cognitive and social constructs in age-restricted bands would increase confidence in the findings. Another limitation of the current study is that although the face region preference paradigm has been used commonly in infants and preschool-aged children, the social preference task has been validated in infants only. Thus it may have lacked the developmental appropriateness to adequately assess social attention in toddlers and preschool children where the social brain is developing rapidly. Repeated study with a larger sample size would allow a focused examination of developmentally stricter age bands. Nevertheless, the findings here suggest that the task assesses social maturity in infants and toddlers, and, with development, could be used to identify CWEOE who may be at risk of social problems. Furthermore, this study explored eye movements in CWEOE near the onset of their epilepsy, which suggests that eye tracking could be a promising tool for identifying young children at risk of social problems at the start of the disease. Future research should expand on this and explore age-related differences in social attention by increasing social complexity in task design, and further explore epilepsy-related variables such as seizure control.

In conclusion, the social attention tasks used here are the first in CWEOE, and the data here provide a platform for future research in CWEOE. The findings have provided evidence of abnormal social attention in this developmentally vulnerable population where social problems are a hallmark of the disease.<sup>12</sup> Eye tracking provides a promising tool toward detecting children at risk of early social functioning problems close to or at epilepsy diagnosis, as well as furthering our understanding of the pathogenesis of these social problems in children with epilepsy.

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## CONFLICT OF INTEREST

None of the authors has any conflict of interest to disclose. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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## REFERENCES

1. Hunter MB, Yoong M, Sumpter R, Verity K, Shetty J, McLellan A, et al. Neurobehavioral problems in children with early-onset epilepsy: a population-based study. *Epilepsy Behav.* 2019;93:87–93.
2. Rantanen K, Timonen S, Hagström K, Hämäläinen P, Eriksson K, Nieminen P. Social competence of preschool children with epilepsy. *Epilepsy Behav.* 2009;14(2):338–43.
3. Brooks R, Meltzoff AN. Connecting the dots from infancy to childhood: a longitudinal study connecting gaze following, language, and explicit theory of mind. *J Exp Child Psychol.* 2015;130:67–78.
4. Mundy P, Block J, Delgado C, Pomares Y, Van Hecke AV, Parlade MV. Individual differences and the development of joint attention in infancy. *Child Dev.* 2007;78(3):938–54.
5. Vaughan Van Hecke A, Mundy PC, Acra CF, Block JJ, Delgado CEF, Parlade MV, et al. Infant joint attention, temperament, and social competence in preschool children. *Child Dev.* 2007;78(1):53–69.
6. van Rijn S, Urbanus E, Swaab H. Eyetracking measures of social attention in young children: how gaze patterns translate to real-life social behaviors. *Soc Dev.* 2019;28(3):564–80.
7. Salley B, Colombo J. Conceptualizing social attention in developmental research. *Soc Dev.* 2016;25(4):687–703.
8. Goren CC, Sarty M, Wu PY. Visual following and pattern discrimination of face-like stimuli by newborn infants. *Pediatrics.* 1975;56(4):544–9.
9. Perra O, Gattis M. The control of social attention from 1 to 4 months. *Br J Dev Psychol.* 2010;28(Pt 4):891–908.
10. Falck-Ytter T, Bolte S, Gredeback G. Eye tracking in early autism research. *J Neurodev Disord.* 2013;5(1):28. <https://doi.org/10.1186/866-955-5-28>.
11. Boraston Z, Blakemore S-J. The application of eye-tracking technology in the study of autism. *J Physiol.* 2007;581(Pt 3):893–8.

12. Rodenburg R, Stams GJ, Meijer AM, Aldenkamp AP, Deković M. Psychopathology in children with epilepsy: a meta-analysis. *J Pediatr Psychol*. 2005;30(6):453–68.
13. Reilly C, Atkinson P, Das KB, Chin RFMC, Aylett SE, Burch V, et al. Neurobehavioral comorbidities in children with active epilepsy: a population-based study. *Pediatrics*. 2014;133(6):e158–63.
14. Suren P, Bakken IJ, Aase H, Chin R, Gunnes N, Lie KK, et al. Autism spectrum disorder, ADHD, epilepsy, and cerebral palsy in Norwegian children. *Pediatrics*. 2012;130(1):e152–8.
15. Karatekin C. Eye tracking studies of normative and atypical development. *Dev Rev*. 2007;27(3):283–348.
16. Wilson CE, Brock J, Palermo R. Attention to social stimuli and facial identity recognition skills in autism spectrum disorder. *J Intellect Disabil Res*. 2010;54(12):1104–15.
17. Fletcher-Watson S, Leekam SR, Benson V, Frank MC, Findlay JM. Eye-movements reveal attention to social information in autism spectrum disorder. *Neuropsychologia*. 2009;47(1):248–57.
18. Chawarska K, Shic F. Looking but not seeing: atypical visual scanning and recognition of faces in 2 and 4-year-old children with autism spectrum disorder. *J Autism Dev Disord*. 2009;39(12):1663–72.
19. Farzin F, Rivera SM, Hessel D. Brief report: visual processing of faces in individuals with fragile X syndrome: an eye tracking study. *J Autism Dev Disord*. 2009;39(6):946–52.
20. Telford EJ, Fletcher-Watson S, Gillespie-Smith K, Pataky R, Sparrow S, Murray IC, et al. Preterm birth is associated with atypical social orienting in infancy detected using eye tracking. *J Child Psychol Psychiatry*. 2016;57(7):861–8.
21. Lunn J, Donovan T, Litchfield D, Lewis C, Davies R, Crawford T. Social attention in children with epilepsy. *Brain Cogn*. 2017;113:76–84.
22. Djukic A, McDermott MV. Social preferences in Rett syndrome. *Pediatr Neurol*. 2012;46(4):240–2.
23. Djukic A, Rose SA, Jankowski JJ, Feldman JF. Rett syndrome: recognition of facial expression and its relation to scanning patterns. *Pediatr Neurol*. 2014;51(5):650–6.
24. Blakemore S-J. The developing social brain: implications for education. *Neuron*. 2010;65(6):744–7.
25. Grossmann T. The development of social brain functions in infancy. *Psychol Bull*. 2015;141(6):1266–87.
26. Gillespie-Smith K, Boardman JP, Murray IC, Norman JE, O'Hare A, Fletcher-Watson S. Multiple measures of fixation on social content in infancy: evidence for a single social cognitive construct? *Infancy*. 2016;21(2):241–57.
27. Hoehl S, Striano T. Neural processing of eye gaze and threat-related emotional facial expressions in infancy. *Child Dev*. 2008;79(6):1752–60.
28. Leppanen JM, Moulson MC, Vogel-Farley VK, Nelson CA. An ERP study of emotional face processing in the adult and infant brain. *Child Dev*. 2007;78(1):232–45.
29. Murray IC, Fleck BW, Brash HM, MacRae ME, Tan LL, Minns RA. Feasibility of saccadic vector optokinetic perimetry: a method of automated static perimetry for children using eye tracking. *Ophthalmology*. 2009;116(10):2017–26.
30. Buswell GT. *How People Look at Pictures: A Study of the Psychology of Perception in Art*. Chicago, IL: The University of Chicago Press; 1935.
31. Just MA, Carpenter PA. A theory of reading: from eye fixations to comprehension. *Psychol Rev*. 1980;87(4):329–54.
32. Meghanathan RN, van Leeuwen C, Nikolaev AR. Fixation duration surpasses pupil size as a measure of memory load in free viewing. *Front Hum Neurosci*. 2014;8:1063.
33. Pannasch S, Schulz J, Velichkovsky BM. On the control of visual fixation durations in free viewing of complex images. *Atten Percept Psychophys*. 2011;73(4):1120–32.
34. Riby DM, Hancock PJ. Viewing it differently: social scene perception in Williams syndrome and autism. *Neuropsychologia*. 2008;46(11):2855–60.
35. Helo A, Pannasch S, Sirri L, Rämä P. The maturation of eye movement behavior: scene viewing characteristics in children and adults. *Vision Res*. 2014;103:83–91.
36. Kiselev S, Espy KA, Sheffield T. Age-related differences in reaction time task performance in young children. *J Exp Child Psychol*. 2009;102(2):150–66.
37. McKone E, Crookes K, Jeffery L, Dilks DD. A critical review of the development of face recognition: experience is less important than previously believed. *Cogn Neuropsychol*. 2012;29(1–2):174–212.
38. Gomez-Ibanez A, Urrestarazu E, Viteri C. Recognition of facial emotions and identity in patients with mesial temporal lobe and idiopathic generalized epilepsy: an eye-tracking study. *Seizure*. 2014;23(10):892–8.
39. Golouboff N, Fiori N, Delalande O, Fohlen M, Dellatolas G, Jambaqué I. Impaired facial expression recognition in children with temporal lobe epilepsy: Impact of early seizure onset on fear recognition. *Neuropsychologia*. 2008;46(5):1415–28.
40. Lunn J, Lewis C, Sherlock C. Impaired performance on advanced Theory of Mind tasks in children with epilepsy is related to poor communication and increased attention problems. *Epilepsy Behav*. 2015;43:109–16. <https://doi.org/10.1016/j.yebeh.2014.11.010>
41. Meletti S, Benuzzi F, Cantalupo G, Rubboli G, Tassinari CA, Nichelli P. Facial emotion recognition impairment in chronic temporal lobe epilepsy. *Epilepsia*. 2009;50(6):1547–59.
42. Uljarevic M, Hamilton A. Recognition of emotions in autism: a formal meta-analysis. *J Autism Dev Disord*. 2013;43(7):1517–26.
43. Bar-Haim Y, Shulman C, Lamy D, Reuveni A. Attention to eyes and mouth in high-functioning children with autism. *J Autism Dev Disord*. 2006;36(1):131–7.
44. Rutherford MD, Towns AM. Scan path differences and similarities during emotion perception in those with and without autism spectrum disorders. *J Autism Dev Disord*. 2008;38(7):1371–81.
45. Speer LL, Cook AE, McMahon WM, Clark E. Face processing in children with autism: effects of stimulus contents and type. *Autism*. 2007;11(3):265–77.
46. Jones W, Carr K, Klin A. Absence of preferential looking to the eyes of approaching adults predicts level of social disability in 2-year-old toddlers with autism spectrum disorder. *Arch Gen Psychiatry*. 2008;65(8):946–54. <https://doi.org/10.1001/archpsyc.65.8.946>
47. Charman T, Baird G, Simonoff E, Chandler S, Davison-Jenkins A, Sharma A, et al. Testing two screening instruments for autism spectrum disorder in UK community child health services. *Dev Med Child Neurol*. 2016;58(4):369–75.
48. Eom S, Fisher B, Dezort C, Berg AT. Routine developmental, autism, behavioral, and psychological screening in epilepsy care settings. *Dev Med Child Neurol*. 2014;56(11):1100–5.
49. Baron IS, Anderson PJ. Neuropsychological assessment of pre-schoolers. *Neuropsychol Rev*. 2012;22(4):311–2.
50. Berg AT, Berkovic SF, Brodie MJ, Buchhalter J, Cross JH, van Emde BW, et al. Revised terminology and concepts for

organization of seizures and epilepsies: report of the ILAE Commission on Classification and Terminology, 2005–2009. *Epilepsia*. 2010;51:676–85.

## **SUPPORTING INFORMATION**

Additional supporting information may be found online in the Supporting Information section.

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